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EDITORIAL

"THE NEW PHARMACOPOEIA"

FOR more than a hundred years the pharmacists of this country have looked forward every ten years to "a new Pharmacopœia." They have done this with interest and with pride, for it has been their greatest single contribution to public health and to the development of their profession. Today they are all aware that almost revolutionary things have happened in the past nine years both in the demands upon the services of the Pharmacopœia and also with respect to its extent of use and its authority.

When the original volume became official in 1936 and was known as the "U. S. P. XI" it was not, in appearance, unlike the Pharmacopœias of the past thirty years, but it was basically different. From occupying the static position of a stabilized authority for a ten-year period, which had been its assumed status in the past, it suddenly took upon itself the progressive, virile, leadership of an up-to-date standard for the medicines used today.

This new place occupied by "The New Pharmacopœia" has been somewhat disturbing both to those who have looked upon it as a sort of Rock of Gibraltar, not to be changed or even challenged as an authority for a decade, and equally so to those disposed to discredit and discount it as an authority because of their claim that "it is always out-of-date."

"The New Pharmacopœia" may today truly be accepted for its leadership; it has taken the initiative in many fields and is alive and ready to accept every challenge of the medical profession for necessary standards.

Only a brief glance at the accomplishments of the decade indicate the remarkable extent of this new program:

The First (1937) and Second (1939) U. S. P. XI Supplements—This policy has demanded two "Supplements" within three years. There are a number of new, up-to-the-minute, therapeutic agents now official through this new policy.

The U. S. P. XI Revision—Never before in a pharmacopœial decade has a Committee of Revision rendered more able or loyal service. Certainly it may be said without dispute that there have never been such exacting demands upon their knowledge or wisdom. The most competent experts obtainable have been continuously challenging and testing the conclusions they have reached as embodied in the

official monographs. Furthermore, their work has continued actively throughout the entire revision period. In other revisions the major service of members of the Committee ended when the book appeared and there was always about five years of inactivity.

That this service is given voluntarily by men of great ability who are already engaged in other active and responsible duties in their regular college or industrial affiliations, is one of the features of the Pharmacopœia which commands the admiration and respect of the medical and pharmaceutical professions and of the officials of the United States Government.

Vitamin Standardization—The U. S. P. has brought order out of chaos for Vitamins A and D and now for Vitamin B_1. This was accomplished by coordinating all scientific vitamin activities in this country and by collaborating with the international authorities in the establishment of U. S. P. standards and biological assay methods.

Anti-anemia Preparations—Through the aid of the U. S. P. Anti-anemia Preparations Advisory Board practically all anti-anemia preparations from liver, now sold in this country, are evaluated and assigned their potency in terms of U. S. P. units, by the Pharmacopœia. No preparation of this type may be imported without having such evaluation.

Surgical Products—The Pharmacopœia Committee, with the aid of an Advisory Board of experts, has been able within the last two or three years to establish standards for surgical sutures and surgical cotton, and will soon announce standards for surgical gauze, bandages, adhesive plaster and other surgical aids. This has been accomplished with the united assistance and approval of every interest, including the Government, the medical and surgical societies, and the manufacturers. The activity includes standards for sterile products for parenteral administration.

Hormones—Again with the aid of an Advisory Board of experts the Pharmacopœia is establishing the standards for this country for important new sex hormones and for other hormones.

Digitalis Standardization—No one Pharmacopœial subject has called for more extensive investigation than this. The U. S. P. is carrying out a three-year international program on the deterioration of Digitalis and its preparations involving clinical and biological tests. Some idea of the extent of this study is indicated by the fact that about 300,000 tablets and 7,000 bottles of Tincture are involved.

The U. S. P. has also undertaken within the past month another study of assay methods and assay standards in which twelve labora-

tories are cooperating, including the Government, universities, private, and industrial laboratories.

The Pharmacopœia and the Physician—One of the most important developments of the Pharmacopœia today is in the many efforts being made to extend information to physicians concerning its value and use. Important among these is the series of special articles appearing regularly in the Journal of the American Medical Association, entitled, "The Pharmacopœia and the Physician." Twenty-eight of these articles have already appeared and the first twenty-four, constituting the "First Series," have also been published in Spanish in the Pan American Sanitary Bulletin. These have been distributed widely throughout the twenty associated Republics of the Central and South American countries. The articles of the "First Series" will also be published in book form, both in English and Spanish, and they are already accepted in many medical schools, in hospitals and by practicing physicians as authoritative therapeutic guides.

The extending of pharmacopœial information to physicians at conventions and by personal interview is also becoming one of the most intensive activities of the professionally-minded pharmacists of this country and is increasing to a remarkable degree.

U. S. P. Preservation and Packaging Specifications—Under the new Food, Drug and Cosmetic Act the requirements of the U. S. P., for preserving and packaging official products, must be maintained. This new responsibility of the U. S. P. has been made the basis for extensive studies and these are among the outstanding researches now under way.

U. S. P. Reference Standards—During the 1920-1930 decade the Food and Drug Administration voluntarily undertook the distribution of several standard U. S. P. preparations for use as a basis for comparison in official bio-assays. This service was greatly appreciated, but because of the cost and the need for increased activity in enforcement work, the department was compelled to discontinue this service.

In 1930 the Pharmacopœia undertook to supply this need and with the aid of members of the Committee of Revision, the assistance of the U. S. P. Vitamin Advisory Board, the Hormone Advisory Board, and with the active cooperation of the technical staffs of chemical and pharmaceutical firms, a number of U. S. P. Reference Standards have been provided. At the present time these are required in the assays of Cod Liver Oil, Activated Ergosterol in Oil, Thiamine Hydrochloride (Vitamin B_1) in preparations, Ascorbic

Acid (Vitamin C) in preparations, Ergot, Digitalis, Aconite, Posterior Pituitary, Strophanthin, Pepsin, and the Solution of Epinephrine Hydrochloride.

Reference Standards for Estrone and also for the Anterior Pituitary-like Hormone are also available, and the preparation of Reference Standards for Estradiol Benzoate, Progesterone, and Androsterone are under way.

That the sale of these Reference Standards has amounted to more than $12,000 during this decade is an indication of the extent and importance of this new Pharmacopœial service.

The U. S. P. Standard for Chemical Reagents and Test Solutions—These sections of the U. S. P. XI and the Second Supplement have given to reagents exacting standardization and, under the new Federal Food, Drug and Cosmetic Act, they now have official standing. This is of great importance not only to chemists interested in medicinal products but also to all chemists in other fields, since it establishes, for the first time, authoritative standards for reagents.

The U. S. Pharmacopœia, Twelfth Revision—No one can predict precisely just what may happen before the U. S. P. XII is published, but well-developed plans seem to indicate that there will be as notable changes in the Twelfth Revision as have revolutionized the U. S. P. XI in the past five years.

The general plan seems to indicate the publication of the U. S. P. XII by 1941, with many advanced features and then another U. S. P. by 1946 (five years later). There will no doubt be a "Supplement" between the two Pharmacopœias. This seems necessary if the U. S. P. is to fulfill its obligations and maintain its place as the national authority for medicines. An interesting proposal is the inclusion in the original book of an "order coupon" for the "Supplement," which will then be sent without charge to the owners of the original copies of the U. S. P. XII. The price of the Pharmacopœia would of course cover the cost of the "Supplement."

The Present Pharmacopœia—Many physicians and pharmacists are just awakening to the realization that the "U. S. P. XI" is no longer a single volume. To have in one's possession "the latest Pharmacopœia" it is necessary to have three volumes, that is, the original U. S. P. XI, which became official on June 1, 1936, the "First U. S. P. XI Supplement," which has been official since December 1, 1937, and the new "Second U. S. P. XI Supplement," which has just been issued.

E. FULLERTON COOK

ORIGINAL ARTICLES

THE MISCIBILITY OF WATER IMMISCIBLE COAL-TAR DISINFECTANTS

(The Efficiency of Sulfonated Castor Oil Mixtures)

By Louis Gershenfeld and Bernard Witlin*

VARIOUS methods are employed in practice for making water-immiscible phenolic disinfectants water soluble or water miscible. Most of the effective methods are time consuming and costly. Satisfactory work has been done upon the preparation of isomeric cresol mixtures ($C_6H_4OHCH_3$) by saponification, employing complex formulæ (1) (2). Oils such as cotton seed, linseed, corn, soya bean, peanut, minahidin, castor, cocoanut, olive, palm and oleic acid have been employed in soap bases on a commercial scale as the agents for making water immiscible products miscible. The addition of diethylene glycol and alkali is also used in industrial processes. Economical formulæ for household and farm use have been attempted by employing soft soap (2), and cheap soap substances (3). Numerous other attempts to make water-immiscible phenolic disinfectants water soluble have been made, but where economy was found, the usual efficiency, both bactericidal and physico-chemical, was affected.

The saponification methods require the boiling of the proper proportion of the several ingredients until a water-miscible product is the result. None, however, offer a method whereby the ingredients, as available, could be placed in one container, mixed by agitation or slight stirring and then be ready, or be kept indefinitely until ready for use by diluting with water.

The Use of Sulfonated Castor Oil

During an experimental investigation with sulfonated castor oil

inner-sulfo

$$(-CH_2-\underset{\displaystyle OSO_2OH}{\underset{|}{CH}}-CH_2-),$$

it was found that water immiscible coal-tar disinfectants were soluble in this oil and the resultant mixture was miscible with water. Sulfonated oils as commercially available are designed as 50 per cent.** and 75 per cent. (4), (5), (the per-

*From the Department of Bacteriology, Philadelphia College of Pharmacy and Science.

**The market price for commercially prepared 50 per cent. sulfonated castor oil is $0.075 per lb. in carboys and $0.09 in smaller quantities.

centage referring to the amount of original oil present). In the laboratory they may be prepared on a small scale as follows: To 100 grams castor oil slowly add from a burette, 35 grams H_2SO_4 (66 Bé). Stir constantly placing the container in an iced bath (45° F.), keeping the temperature of the mixture at 70 degrees F. Wash with 135 grams 20 per cent. sodium sulfate (for stiffer oils use acetic anhydride) in a separatory funnel. Allow to stand for 24 hours in the separatory funnel. Drain off the acid water and neutralize with caustic soda (28 Bé), using methyl red as the indicator (one drop of the indicator for 25 cc. of the oil). This yields the 75 per cent. sulfonated castor oil. For the preparation of 50 per cent. sulfonated castor oil, water is added in proportion to the fat content, and caustic soda is added until a faint reaction is obtained with phenolphthalein (pH 8.3 to 8.5).

The 50 per cent. sulfonated castor oil was found to be satisfactory for preparing a mixture with water-immiscible coal-tar disinfectants, resulting in a water miscible mixture. The hydrogen-ion concentration of the sulfonated castor oil plays an important role in the preparation of this mixture. It must possess an alkaline reaction to phenolphthalein and the pH is to be between 8.3 to 8.5.

Experimental Investigation

The following chemicals were investigated:

(1) *o*-cresol; (2) *m*-cresol; (3) *p*-cresol; (4) Cresol (U S. P.); (5) (15%) Tar Acid Oil; (6) (25%) Tar Acid Oil; (7) High Boiling Point Tar Acid Oil; (8) Resorcinol; (9) Hexylresorcinol; (10) Orthophenylphenol; (11) Chlor-symmetrical Xylenol; (12) Chlorthymol; (13) parachlormetacresol; (14) Salicylic acid; (15) Betanaphthol; (16) Creosote; and (17) Guaiacol.

Miscibility

All of the liquids (cresols, tar acid oils, etc.) were capable of mixing with the 50 per cent. sulfonated castor oil in all proportions. Such mixtures were miscible with water even when using only ten parts of the 50 per cent. sulfonated castor oil and 90 parts of either ortho, meta, para or tri-cresol, and (15%) or (25%) tar acid oils. The high boiling point tar acid oil required 50 parts of the 50 per cent. sulfonated castor oil to become water miscible. The solids were all soluble in concentrations as high as 50 per cent., but in most cases

necessitated slight warming to go into solution. In the case of the ortho, meta, para and tri-cresols clear aqueous solutions were obtained, while milky solutions resulted when using the tar acid oils. The only objectionable observable macroscopic change was apparent in the case of resorcinol and hexylresorcinol, where a reddish color was produced due to the reduction of the phenolic group present therein.

Bactericidal Efficiency

All solutions were tested for bactericidal efficiency, using the phenol coefficient technique and employing the United States Food and Drug Administration procedure (6) with *Eberthella typhi* at 20 degrees C. as the test organism.

Dilutions required were prepared with sterile distilled water.

Findings

It was found that the more phenolic compound present the higher was the bactericidal efficiency (Table 1). The efficiency of the bactericidal agents in the 50 per cent. sulfonated castor oil, or when emulsified by the U. S. P. XI (2) method was identical † provided the amount of the active bactericidal agent was constant.

TABLE 1

Disinfectant	Parts of Bactericide in Solution	Parts Sulf. Castor Oil	Phenol Coeff. *E. typhi* at 20° C.
Cresol U. S. P.	40	60	1.18
Cresol U. S. P.	50	50	2.20
Cresol U. S. P.	60	40	2.80
Cresol U. S. P.	70	30	3.00
Cresol U. S. P.	80	20	3.62
15% Tar Acid Oil	40	60	1.62
15% Tar Acid Oil	50	50	3.30
15% Tar Acid Oil	60	40	3.71
15% Tar Acid Oil	70	30	4.74
15% Tar Acid Oil	80	20	6.33
15% Tar Acid Oil Saponified according to U. S. P. XI Method			3.30

† The method given by the United States Pharmacopœia XI employs 50 per cent. of the active ingredient. (One pound of the active ingredient makes two pounds of the finished product, upon saponification with linseed oil, sodium hydroxide, potassium hydroxide and water.)

TABLE 2

Disinfectant	Mixture		Phenol Coeff. *E. typhi* at 20° C.
	Parts Bactericide grams or cc.	Parts Sulf. Castor Oil	
Cresol (U. S. P.)	50	50	2.20
o-Cresol	50	50	2.20
m-Cresol	50	50	2.45
p-Cresol	50	50	2.75
15% Tar Acid Oil	50	50	3.30
25% Tar Acid Oil	50	50	6.33
High B. P. Tar Acid Oil	50	50	18.20
Resorcinol	50	50	1.10
Hexylresorcinol	50	50	43.66
Orthophenylphenol	50	50	1.75
Chlor-symmetrical Xylenol	50	50	67.00
Chlorthymol	50	50	80.25
Parachlormetacresol	50	50	28.35
Salicylic Acid	50	50	0.66
Betanaphthol	50	50	0.70
Creosote	50	50	1.66
Guaiacol	50	50	1.25
50% Sulfonated Castor Oil	00 Control	100 Control	0.00

Summary

(1) A method is presented for increasing the water solubility or miscibility of water immiscible coal-tar disinfectants commonly used.

(2) A rapid, convenient, economical and efficient method for making coal-tar and phenolic disinfectants water-miscible may be accomplished by mixing with 50 per cent. sulfonated castor oil (pH 8.3 to 8.5).

(3) The bactericidal efficiency of these mixtures is governed by the amount of the active bactericide present and is directly proportional to such concentration.

Conclusion

Since no toxicity tests have been conducted upon these preparations, it is suggested that mixtures of 50 per cent. sulfonated castor oil and water immiscible coal-tar disinfectants be used for the present, only as general disinfectants, as required for the disinfection of floors, toilets, medical and surgical instruments, in laundries, etc.

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(3) Buckley, J. S., and Bunyea, H.: "Diseases of Parasites of Poultry." *U. S. Dept. Agr. Farmers' Bulletin,* p. 1652 (1931).

(4) Gruen and Woldenberg: *J. Amer. Chem. Soc., 31,* 490 (1909).

(5) Herbig: "The Oele und Fette in der Textilindustrie." Second ed., p. 253 (1929).

(6) Circular 198, Food and Drug Administration, United States Department of Agriculture, December, 1931.

Calcium Acetylsalicylate. I. Gellman. *Mfg. Chem. 10,* 5 (1939), through *Quart. J. Pharm. & Pharmacol. 12,* 282 (1939). Calcium acetylsalicylate is subject to hydrolysis due to its water of crystallization forming polysalicylides as well as calcium salicylate and acetic acid. This hydrolysis is prevented by the addition of about 5 per cent. calcium chloride. The stabilized powder has about the same stability of acetylsalicylic acid and it may be prepared as follows: Suspend 90 gm. of finely powdered acetylsalicylic acid in 126.6 gm. of 40 per cent. w/v solution of calcium chloride. A suspension of 26 gm. of precipitated calcium carbonate in 300 cc. of the calcium chloride solution is added with stirring and the mixture warmed to 50 degrees C. until frothing ceases (about 3 hrs.). The paste is then filtered under pressure washed with 200 gm. of the solution of calcium chloride drained well and dried *in vacuo* at 60 degrees C. The product contains 5-7 per cent. calcium chloride.

Tablets of the stabilized powder may be prepared by granulation by the use of high pressure, employing a special compressor hopper in constant motion containing a discharging rotor to fill the matrices and using highly polished punches made of a non-ferrous alloy to avoid the need for a lubricant. Starch of low moisture content may be added as a disintegrating agent.

Tablets so prepared are readily soluble in water, giving a neutral tasteless solution. The pharmacological properties of acetylsalicylic acid and its stabilized calcium salt are summarized. L. F. T.

THE NEW "SECOND U. S. P. XI SUPPLEMENT"

THE second Pharmocopœial Supplement is now ready for distribution. It includes new monographs for Ascorbic Acid, Cyclopropane, Mandelic Acid, Methyrosaniline Chloride, Nicotinic Acid, Purified Cotton, Soluble Pentobarbital, Sulfanilamide, Surgical Gut or "Catgut," Thiamine Hydrochloride, Tribasic Calcium Phosphate, Tribasic Magnesium Phosphate, Natural Vitamin A in Oil, and Natural Vitamins A and D in Oil, official in the U. S. P. for the first time. Two of these substances, Tribasic Calcium Phosphate, and Methylrosaniline Chloride, were in the National Formulary but these new U. S. P. standards now supersede the corresponding standards of the N. F. VI. There is also a revision of 85 of the monographs of the original U. S. P. XI, the revision of Antipneumococcic Serum including the recognition for the first time of Types II, V, VII, and VIII. Under Tetanus Antitoxin, the use of animals other than the horse are permitted, while under Diphtheria Toxoid, the Alum Precipitated form is given official recognition. It also contains a new bio-assay method for Thiamine Hydrochloride (Vitamin B_1). Improved assays for Vitamin A and Vitamin D are also given.

A cumulative index lists all U. S. P. titles and indicates where the present official monograph now in force may be found. This index emphasizes the fact that the "U. S. P. XI" now consists of three volumes—the original U. S. P. XI, which became official on June 1, 1936, the "First U. S. P. XI Supplement" official December 1, 1937, and the "Second U. S. P. XI Supplement" which will become official January 1, 1940, with the exceptions indicated below.

In the new Supplement the following exceptions are made for the revised monographs for Cod Liver Oil and Nondestearinated Cod Liver Oil and for the new monograph providing standards for "Surgical Gut" or "Catgut." These three texts do not become official until July 1, 1940, six months additional time being allowed for the adjustment of labels and existing stocks.

Of particular interest to pharmacists is the requirement that the regular bottles of Solution of Magnesium Citrate shall contain not less than 340 cc. and not more than 360 cc. Absorbent cotton is required to have a certain minimum fiber length and to be sterile.

The Second U. S. P. XI Supplement, which is larger than the First Supplement, is $1.50 prepaid. Pharmacists and others should obtain this volume in order to acquaint themselves with the changes which become official on January 1, 1940.

EXAMINATION OF PHARMACISTS FOR THE MEDICAL ADMINISTRATIVE CORPS, REGULAR ARMY

THE War Department is announcing an examination November 13-17, 1939, both dates inclusive, to qualify candidates for appointment as Second Lieutenant in the Medical Administrative Corps, Regular Army, to fill the five existing vacancies.

Appointments will be made from pharmacists, male citizens of the United States, between the ages of twenty-one and thirty-two years, who are graduates of recognized schools or colleges of pharmacy, that is, schools or colleges approved by the American Association of Colleges of Pharmacy, requiring four years of instruction for graduation and legally authorized to confer the degree of Bachelor of Science in Pharmacy.

Examination for appointment includes physical, a written examination in Practice of Pharmacy, Pharmaceutical Chemistry, Pharmacognosy, Pharamacology, and Bacteriology, Hygiene and Sanitation, and an estimate of the candidate's adaptability for military service.

Examining boards will be convened at convenient locations throughout the continental limits of the United States for the examination of candidates authorized by the War Department to appear before them. Full information and application blanks will be furnished upon request by The Adjutant General, War Department, Washington, D. C.

Applications will not be considered after October 28, 1939.

CRYSTAL GAZING*

Ivor Griffith, Sc. D., Ph. M.

FOR several days the lecturer has impatiently, though with some fear and trembling, awaited this occasion so that he might, in the presence of his audience, duly and properly apologize for the choice of so specious, so misleading a title. And to add to his dire dilemma, comes now a realization that he has chosen the first of April—the fools' own holiday—to perpetrate so unholy a hoax. He does not know, even now, what proportion of his audience came to listen to a dissertation on crystal gazing—involving that which might be esoteric, cabalistic, arcane, hermetic, magic and mystic. To such he now makes the disappointing announcement that in this contemplation of crystal gazing there is neither necromancy nor lithomancy. The lecturer has consulted neither the Oracles of Zoroaster nor the Seven Stewards of Heaven—Arathron, Bethor, Phaleg, Och, Hazith, Ophiel and Phul—in their chariots of cirrhic clouds.

In short—the lecture has none whatever to do with clairvoyance or magic. Not indeed, that such a presentation would not be popular—for even in these learned days—the dumb and the dumber are still much with us. There are still those who foolishly believe that benedictions and banalities are both born of the stars—still those who like their dreams done "medium", and plenty more who seek their fortunes in tea leaves and ten-spots and trust their birthdays, not their birthrights, to redeem their souls.

SYSTEMATIZED IGNORANCE

Sciosophy or systematized ignorance—that most delightful science in all the world, because it is acquired without labor or pains, and keeps the mind from melancholy—is still the popular science, and its votaries are legion.

And so do we conclude our odd apology—not for the legend or substance of our lecture as we know it to be—but for the inference involved—namely, that any lecturer in this course might have been charged with selecting so inane, so asinine and so undivine a topic—as *Crystal Gazing;* unless—unless—the lecturer at the conclusion of his evening's presentation might have done what Dr. LaWall did when he lectured on the "Romance of the Occult"—terminating a learned and comprehensive address in the never to be forgotten, illustrious and high sounding aphorism of a famous cartoonist—"It's the bunk."

*A Popular Science Lecture, delivered at the College.

And so the crystal into which we shall together gaze this night is neither an instrument of the devil nor a playtoy for fools. Rather it is the very material, many-edged, many-faced, stream-lined state, self assumed by certain forms of matter.

THE VERSATILE CRYSTAL

Actually it is a merry conceit that motivates anyone who attempts of expects else than a cursory rambling discussion upon the vast subject of the crystal—within the compass of an hour or so. Indeed this is a subject that has a voluminous literature all of its own. Tomes over tomes have been written about its multifarious facets. Its mathematics have intrigued even Einstein himself. Through its clear spy-glass our modern physicists are learning the structure of atoms. X-ray experts have found it a tool not a toy. Radio engineers pay tribute to its versatility, by tickling its face to incite it to sound. Optical devices use it to make light rays walk the straight and narrow path. Automotive engineers fear it—for they know that stress and strain on metal structures change their pliant state to a brittle crystal—and the broken spring or fractured cylinder is dismal evidence of such a change.

The "frolic architecture of the snow"—and ice that binds the babbling brook with a December dumbness, is only other evidence of Nature "going" crystal. Minerals tight-locked in embrace of earth—the sparkling diamond sprinkled to our planet when other worlds cracked up in meteoric splendor—emeralds and rubies, sapphires and amethysts that with their kaleidoscopic aura make the dawdling dowager look like a strutting chandelier; the stalactites and stalagmites of the eerie dungeon—all are crystal creations—all are patterns of nature in her best acicular mood.

So it is obvious that this brief presentation must contemplate only one or two angles of the crystalline structure. And one of the angles which we have chosen for such discussion are those reflected in the lines of a rambling letter, sent some time ago, to one who had lived long and intimately with the sciences—and who even in the declining years of his useful life—listened with tolerance to the murmurings of immature minds.

I refer to the late Professor John Uri Lloyd of Cincinnati, one of the acknowledged pioneers in the now expanded field of colloid chemistry—and who up to his last conscious moment, continued to display a philosophy, a faith, a religion built upon the demonstrable in nature

and not upon the interpolated texts of scientific cook book compilers. The letter considers the crystal—not the cell as being the beginning—the very bottom step in the long-long trail of evolution. Long before the first Darwinian monkey scraped his shinbones sliding down the prehistoric pine in his haste to achieve to manhood, life was already evolved and involved. The origin of the species was a much simpler organization than the monkey or the jelly fish or even the amœba.

But before reading excerpts from this letter let it be understood by all, that the crystal is not a thing, but a state,—a manner of being,—a definite form assumed by matter and as such possessing properties unique and peculiar to such structure. This is exactly as with the colloid, that morphic system antonym of the crystal. For the colloid too, in spite of our lingering misconceptions, is only a state of existence, and not a class or group of material bodies. Actually the difference between colloid and crystalloid might be superficially explained by stating that a crystal is an edifice built by a community of symmetrically minded indentical atoms or molecules, and is simply a magnified scale of the constellation of the atom or molecule itself, whereas the colloid state finds guilds or groups of identical atoms or molecules not bent on linear symmetry, but drawing new power from group strength, and curving their sinuous way to action and reaction.

CRYSTAL AND COLLOID TOO

It is now known that matter such as common salt, normally existing in the crystal state, can be coaxed to colloid existence, quitting its cubicle for a curve-bound coracle, and displaying brand new physicochemical properties.

But it is the new properties which the colloid state brings to matter that has made colloid chemistry so fertile a field of invention and application during the last decade or so.

In agriculture and in the tanning of leather, in the working of clay for the manufacture of the common brick or for the production of the finest porcelain, in the production of artificial silk and of smokeless ammunition, in the dyeing of textile fibers and in the productions of the blue of the sky or the blue of the eye, the colloidal state of matter plays a part. When, further, we recall that Nature has selected matter in the colloidal state to be the vehicle of life and as the medium in which all living processes take place, the importance and interest of the colloid state which has been wisely called the *twilight zone of matter,* become obvious.

WHEN IS AN INCH AN ACRE?

A simple illustration will suggest the immense powers that are unsealed when matter achieves to the colloid form. Suppose we have a cube of iron measuring an inch on each edge. The total surface would be six square inches. The electrical charge, the magnetic force, is on the surface; therefore the greater the surface the greater the charge; and if we divide the cube of iron into smaller pieces we increase the surface areas. In the colloid condition that iron cube is divided into particles so minute that they are invisible, hence instead of six square inches of surface radiating electric energy, we have something like 127 acres. And that's not a field—it's a farm!

Of course, if we accept our education in the things of science from certain sections of the press, we must learn to take it with a hefty grain of salt. For instance witness the following quotations from a recent popular article on colloids, appearing in one of our so-called digests of current literature.

COLLOIDAL BUNK

"In the Colloidal Laboratories of America they have a motion picture which is as weird as anything ever shown on a screen,—a movie of a headache. The actors are the nerves in a human head, magnified millions of times. You *see* the headache. Those nerve endings are tangled, twisting, writhing. Then you see the colloids enter. These rescuers, smaller than the blood corpuscles themselves, march straight to the spot where there is an *unbalance* of the vital metals. You see those laboratory-prepared colloids restore normalcy there at the seat of the trouble. Then you see the nerves cease their twisting, relax, and assume their proper position. (Shades of Orangeine and Munyon's Headache Wafers!)

"Dr. Steinmetz, the wizard of electricity, devised a method of utilizing colloids in the treatment of sinus trouble. The Bide-a-Wee Home, New York's famous hospital for cats and dogs, can cure mange in three days, where it used to take three months. A large midwestern city was freed from the scourge of goiter when colloidal iodine was added to the water supply. A famous institution for the treatment of alcoholism is experimenting with a colloidal solution of gold which apparently not only overcomes the effects of excessive drinking, but removes the craving for liquor as well." (Please note that we are continuing a quotation.)

"In colloidal form iodine, for example, is one of the elements essential to the well-being of human cells. Yet if you should drink as much as two or three grains of free iodine, it would kill you. A famous colloid expert when explaining this, held up an eight-ounce cup full of colloidal iodine. 'There', he said, 'is the equivalent of 740 grains of free iodine—enough to kill 300 men'—and he drank it!" (End of quotation—but unfortunately not of the "famous colloid expert" whose similar asininities continue to appear in print as a kind of popular science (sic).)

But now to the letter—

"Yet between the colloid and the crystal is to my mind not a line,—but a land— not a spot—but a space, and without a break in continuity, just as between youth and senescence there is not a sharp dividing line but a gracefully declining span.

"And what entrances me about the 'lifeless' crystal is the inanimate activity (if these two words be compatible) occurring in its molecular mobs.

"But what a governed, regulated activity it is. Consider the intimate growth of a clear crystal from the depths of a murky fluid.

"Were our ears attuned to the noise of busy microcosmic entities what clamor would come from that liquid. Could our eyes discern the whirling, seething mob of molecules, they would be blinded with the strange dizziness.

CRYSTAL GROWTH

"Tiny particles, builders of every crystal, dance about in Brownian ecstasy searching frantically for the attractive nucleus.

"Finding it they come to rest beneath its ramparts and from all directions they draw their cohorts to the coalescence and only the proven pure can join the congregation.

"Atom upon atom, particle upon particle, and sheath over sheath the crystal is built gradual, orderly and certain. Finally facet and face and edge, definite in every detail, effect the final form of the pure and perfect crystal.

"And the dross, the foreign and the colloid things are left behind in the flued for only the actual, belonging things find room in the mass of the crystal.

"What a thing of system and sheer symmetry this finished crystal is and how well it knows its geometry. And how well it knows its

own mind. For it rarely, and then only with reason, varies from its ordered major pattern, every component atom sitting gaily by its lattice window—waiting the great adventure.

"It has been stated as a statistical truth that everything strives toward symmetry so far as the environment will allow—an aphorism in which rests not only the way of the crystal but the salvation of mankind as well. But we can ascribe neither instinct nor conscience to the crystal, its symmetric expression is as yet a confidence of atoms—a secret of the lesser infinities.

"For the crystal—in spite of the obvious activity that governed its growth, is called inanimate—dead. Polarity, explains one—another says electronic motivation. But is it? How does the Brownian ecstasy differ from other life? Is it here that Life begins?

"Yet you say that Life is colloid, that Life as it finds expression in us, seemingly abhors the crystal.

LIFE IS COLLOID

"Full of curves is Life, and shy on plane geometry. And truly our bodies do seem to outlaw the crystal. The crystallizable is tolerated; the crystallized is outlawed or ousted.

"Witness the cholesterol crystals of the gall stone, the calculi of kidney or bladder, the uric acid rosettes—the phosphate prism, the heart stone, the eye stone, the bloody bezoar, how the contrivances of the body will either wall them off or will them out.

DEATH IS CRYSTALLINE

"Know that, as man approaches the twilight zone of his short day of stay this side of heaven, the electric forces that had reached their peak at forty, are nigh well spent at seventy. Senescence has brought obsolescence, an obsolescence beyond repair, for life has lost its atomic discipline. Rebellious molecules no longer go their lively colloid way—but choose a crystal destiny. Rocking in his second cradle, the old man surrenders to a linear lullaby that eventually charms him to his long and longed for sleep. Eyes that once had sparkled in liquid ecstasy are dimmed with a dank deposit. Arteries that in days gone by had bulged with wanton abandon when emotion-thrilled blood cells bounced against their sides, are now as unbending and brittle as bars of burnt fudge. The rhythm of his rocking chair keeps time to the tune of cracking arteries, and death will come to him at last—not with its mythical sickle or scythe, but with the poignant points of a million crystal clusters.

"Life as we live it is Colloid—Death as we dread it is crystal.

"Yet withal if ever it be given to man to discover where life started, I deem that it will be found to have started not with the cell—but with the molecule—not with the curve but with the line and the angle—not with the colloid but strangely enough with the crystal."

And what prompted quoting from this rather discursive and inexact letter was reading in a recent issue of *Science,* the following interesting observation of Dr. Vaughan.

"A chemical theory of the origin of species was presented in a paper prepared by Dr. Victor C. Vaughan, formerly head of the Medical School of the University of Michigan, a noted authority on evolution. He goes far back beyond Darwin to a period long before the appearance of the earliest and simplest single-celled plant or animal, which is the point where the biologist begins. For he believes that life is molecular and not cellular. The microscope shows us that cells constitute the structural units of all plants and animals, but Dr. Vaughan thinks that the size and shape of these little bags of protoplasm are less important than the composition of their contents.

"Dr. Vaughan admits that 'up to the present time no chemist has awakened dead matter into life. It may be that this will never be done', but that should not discourage future experimentation in this line.

"Indeed human search for Life's hiding place will continue into the long years. Science will always be asking questions, and continue to progress with its offered answers. Indeed not even the present narrow confines of human intellect shall hinder its onward march. For human intellect itself marches onward with the years.

"Out where eternity starts time was when the only life that existed upon our planet was in the infusoria that floated in the brackish shallow waters of the warm primeval seas, and we are the evolutionary products of these forerunners of all living things. The race of man will some day be as far removed from us as we are far removed from these jellied infusoria. And who today stands bold enough to even dream of man's intellectual capacities at this stage of his evolution?"

A SECRET!

But there there are those who say that even then shall the mystery of Life be sealed from man's understanding. And there are others confident that we are on the edge of tremendous discoveries. The evolutionists, the supporters of mecha-

nistic theories of life, the fundamentalists, all seem to feel their ground secure, and even go so far as to question room for religion in their queer world of science.

But in these hectic days of argument when religion and science seem incompatible and inimical, and when theories of evolution are bandied about in puny human quarrels, it is pleasant to hear a philosopher come out of the wilderness to say, as did MacDougal recently, that science indeed does not destroy, but that it rather justifies, religion.

And in this connection the speaker cannot refrain from mentioning again an episode of his early Sunday school days, when his old physician teacher said that he had always been greatly fearsome of the day when some blundering, scientific idiot would come upon the secret of Life, and so bring on the whole human race the mighty wrath of a Creator whose most precious riddle had been solved by a mere creation called man.

But physicians and scientists of the new and so-called advanced schools think not in this respect, for in our newspapers of a few days ago we read of a Carrel the Physician who in his search for this philosopher's stone, has known how to keep a fragment of a chicken embryonic heart growing and thriving for nearly twenty years, in an artificial atmosphere. Alexis Carrel, this wonderful man of science, is quite able with his invigorating and life-sustaining media, to cause this fragment of embryonic tissue to add cell after cell to its structure, and so rapidly that daily portions must needs be dissected off, so that the tissue growth does not overflow its container. But each cell that divided and gives two to the tissue, only adds to Carrel's dilemma.

DEATH'S ANTIDOTE

As the cells multiply, so do the troubles of Carrel, and the distance to a discernment of the secret of life becomes proportionately further. The secret of life lies not in its promotion and furtherance and sustenance, but rather in its origin. Whence comes this subtle thing called life—not what is Death's antidote? Our old physician Sunday school preceptor was old-fashioned enough to teach us that this latter has been man's to own since a gray morning in Nazareth.

Then there are those who seek to explain the processes of all vital tissues on purely mechanical lines. To those people every movement of our bodies, every concept of our minds, every leaning of our

desires, our inspirations, our hatreds, our loves, our longings, our every phase of action, all are inevitably governed by the ordinary laws of physics and chemistry. These are the people who predict the coming of a day when science will give a chemical formula for Life.

Vernon Kellog has recently stated: "The chemists and physicists keep pushing in on the field of the biologist; they keep claiming more and more share in the telling of what life really is, not what its joys or goal are, but just how being alive is different from not being alive."

He concludes that life is a series of balanced chemical processes, and that when this balance is disturbed by a change in environment one process goes faster than another, and then the living creature grows or decays, thrives or declines, goes on living or dies. It is all a matter of chemistry and the physics thereof.

Yet we wonder, moreover, how anyone with this mechanical conception of life can explain the following fact: How can a single spermatazoon with its cell so minute that fifty million can move freely in a drop of liquid, permit the passage of all the physical and mental peculiarities from father to son, or, by the aid of this single little cell, even skip the son and reappear clearly in the grandson?

Can laws of mechanics explain this?—this remarkable potentiality in a single cell that direct form of motion and modes of development even unto the third and fourth generations? Yes, and even transmit mental and spiritual qualities? Here indeed physics, chemistry and anatomy and histology all turn from the light and point their hopeless fingers into the night. For there are many, many things too close, as yet, and perhaps forever too intimate for man to know and understand.

ADAM OR THE ATOM? EVE OR THE ION?

But let us cease this maddening soliloquy—for whether Adam or the Atom was the primal daddy of us all, whether Eve or Ion mothered all things living, certain it is that life is real—life is earnest—and the grave is never its goal. The poet—if poet—who penned the following querulous, quarrelsome lines—expresses something at least of the dilemma of all who rely on less than Faith to answer the burning question.

Gather—O Cells—rub against each other
In your bed of slime—rub against each other,
Ooze your protoplasmic oil
Warm anointing, cosmic oil
Grease the wheels that rule my head,
Prove to me before I'm dead
With your lush electric thinking

Hush this wild, erratic blinking.
Tell me—tell me—why I am—
Whence I am—What I am—Where I am—Am I?
Did God—if God—out of the Clod
Carve me—His image—out of the sod?
Why did He? How did He? When did He?
Does He at all
Know I exist? Cares He at all
Whether I rise—Whether I fall?
Whether I've been—Here—at all?

Much more comforting is the viewpoint of Sir Alexander Findlay: "Although we must recognize the essential importance of colloidal matter in connection with the phenomena of life, and that matter in the colloidal state is the vehicle of life; although, further, we may interpret much of the behavior of living matter in terms of physics and chemistry, I am of the opinion that we cannot explain life itself in terms of physical science. There seems to be no continuity between inanimate colloidal matter and living matter; but there is a distinct and sharp break in the curve of relations. In other words, life is a new factor, a new set of potentialities, introduced into inanimate matter. Life is a new creation."

But to return to our crystal gazing, viewing it now at another angle. Previously we have said that life abhors, shuns, detests the crystal. The crystallizable it tolerates so long as it is liquid and limpid, but the sharp edge of the formed crystal is to life, in the animal form, only a curse and an abomination.

When air is surcharged with moisture and its temperature is suddenly lowered, April showers come along. By the same token when a solvent, saturated with a soluble crystalline material is cooled—it too rains—a shower of crystals.

Now that is to be expected. But what we do not expect, nor explain, is how it comes to pass that certain body fluids, weak in soluble crystals, deposit those crystals in queer and out of the way places in the anatomic landscape,—and without any rhyme or reason.

THE FAIR, FAT AND FORTY

For instance there is that freakish phenomenon that fancies the fair, the fat and the fortyish—and fills their gall bladders with an assortment of calculi—gallstones that too often grow to be tombstones—and these gall-concretions number anywhere from one to a thousand, and range in size from pinhead to plum.

And they are just as diversified in chemical composition. Cholesterol, that carbon-rich crystalline alcohol, erstwhile a resident of epidermal cells, and a precursor of vitamin D, is the most common ingredient of gallstones. Then comes a compound of lime with bile pigments. Less frequently we find the several salts of calcium, chalk, plaster paris, the phosphate, the oxalate, etc. Traces of copper, iron, zinc and manganese, mercury, silica, globules of fat, uric acid and urates have also been reported present.

One inquisitive surgeon found the nucleus of an oddly shaped gallstone to have been a needle, a fact which should not alarm the modern woman, who rarely sees needles except in the victrola.

These formations generally originate from definite nuclei, usually not of crystalline structure. Masses of epithelia, agglutinated bacteria or small sedimentary clots or masses attract to them concentric layers, of crystal or amorphous fragments. In the words of a modern musical composition the crystals grow around and around, but unfortunately they do not "come out here", but remain there, until the gleeful surgeon opens the subject and bails them out by the handful.

In a country that goes wild over excesses, and glorifies marathon dancers and parents of quintuplets, what shall be said of one Wilhelmina Strossman, of Austria-Hungary, whose excised gall bladder embraced 17,082 rounded gall-concretions, and who after their removal lived at least long enough to count them.

Just what causes gallstones in some and not in others is still a debatable matter. A disorderly diet, infection, vitamin lack, congenital predisposition, electrical deposition, all have been charged as responsible for gallstone formation. How to anticipate or prevent their formation is the province and concern of the physician. Likewise their diagnosis and treatment, which in the main calls for a sharpening of scalpels and some abdominal tailoring.—Although non-surgical treatment occasionally produces results.

THE INQUISITIVE X-RAY

However, the advent of the X-ray with its inquiring technic has simplified the diagnosis of these and other calculi. Some calculi are pervious to the ray, and refuse to reflect their outline on the negative. For such there has been perfected a special technic whereby specific and shadowing chemicals are despatched to the location where the calculi hide. And while these special substances are sitting in chemical comfort around the

concretions, along comes the artist, photographs them, and with them the recalcitrant calculi. Then the surgeon knows beforehand the real site for his cutting technic.

Quack medicines have been offered for the elimination of gallstones. Obviously they can be of no value, and are more commonly dangerous by incurring a postponement of remedial surgery.

One preposterous quack remedy for gallstones offered its treatment in two spasms. Spasm No. 1 was a saponifiable oil, to be consumed on one grand gulp; spasm No. 2 to be taken shortly thereafter was a mild alkali, which when mixed in the gastric churn, with the aforementioned oil, produced gobs of an insoluble soap that looked not unlike gallstones when reclaimed from the excreta of the patient. In other words the quack medicine produced its own fictitious gallstones—and usually much to the satisfaction of the dumb but proud patient.

Heart stones, sized and shaped from pea to bean, are not uncommon, although that busy pump is more apt to show a crystal calcification in its own tissues, notably at the aortal region. Skin concretions occasionally occur in the aged.

BEZOAR STONES Enteroliths or intestinal concretions are fortunately more common in animals than in man. Under the name of bezoar stones they were held in high esteem by the Arabs, especially as charms against the plagues. Later they came into great vogue in Europe. They were supposed to be obtained from the intestines of the Persian wild goat. Others were concretions from the stomachs of apes, formed much as the pearl is formed in the oyster. They are obtained from the animal by giving him an emetic, the primary difficulty being to catch the ape. Bezoar stones were crystal concretions of calcium phosphate built around an organic nucleus. They were used internally in ten to twenty grain doses, or used as lavallieres on a string mostly as antidotes to poison and infections, and some were alleged to be worth ten times their weight in gold. It is said that as late as the 18th century, hundreds of pounds of bezoar stones were sold annually in the apothecaries shops of London. One Scotch commentator of that period sarcastically notes that most of the bezoar stones sold in that city had never seen the inside of a goat or an ape until an Englishman swallowed them.

Eye calculi, pulmonary calculi, pancreatic rhinoliths or nose concretions, salivary stones and bronchial crystal growths are not unsual.

The most common type of a disdained crystal aggregate however is the urinary concretion, forming in the kidney or in the bladder. They too, as the gallstone, are variable in size and in composition, debatable as to causation and formation, and usually a source of dread and discomfort to one unfortunate enough to accumulate such. Their diagnosis is not a matter of great difficulty particularly since the advent of the X-ray, and their cure, especially when large, usually is only by way of the knife, or other surgical implements.

Frequently, however, nature provides for their painful elimination, especially if they remain small and gravelly. Such elimination is generally accompanied by much distress and frequently with loss of blood.

Just how, just why, they form in some and not in others is again a moot question. In Philadelphia most people blame Aqua Philadelphica for causing such calamities, charging that much maligned fluid with being too rich in indescribable solids. Actually there are more potential crystalline solids in one potato than in a whole gallon of Philadelphia water, whether it be of the variety Schuylkilliensis or Delawariensis. And as for those who seek the springs of Fairmount to escape the banalities of spigot water—the joke is on them, for the solid content of the waters of many Fairmount Park springs in quantity and kind, is more and worse than that of our regular water; and especially when those springs draw some of their essence from the carcassy effluvia of the aristocratic cemeteries that monotonize and monopolize the surrounding hills and dales of fair Fairmount.

THE LITHIUM MYTH

Some years ago an enterprising neophyte in chemistry discovered that soluble lithium salts when boiled in a test tube with urinary calculi, of the uric acid and urate type, promptly dissolved them. And immediately thereafter came the lithium craze in medicine. Lithium tablets, lithium waters and lithium in many another form came to be the fashionable gout, rheumatism and kidney stone dissolver par excellence. It did not occur to practitioners that the patient or some of his spare parts had to be boiled in a gargantuan test tube in order to realize the effectiveness of the lithium reaction.

However, it is a strange commentary upon the stubbornness and ignorance of some people that lithium compounds are still prescribed and that lithia tablets are still swallowed by the hundreds.

Gout (podagra) is a constitutional disease alleged to be produced by crystal misbehavior. Sodium urate and other urates deposit on the articular surfaces of the small joints and eventually in the arteries, the heart valves and elsewhere. Nature is usually quite impartial, and while her gallstones are most frequently destined for the speakier sex —the male gets the gout. And the male who adds the insult of alcoholic and dietary excess to the injury of an inactive life; is the common complaining sufferer.

Curiously enough the point of concentration for an attack of gout is the great toe and the helix of the ear, a penalty imposed, according to Paracelsus, for kicking too much and for listening to much that should not be heard. In any event it is more than likely that gout and many of these crystal pathologies start in the kitchen, or the dining-room, and that a rational diet, fitting to the individual, is a safety factor not to be ignored.

If this be so prevention of these calamities incident upon Life's distaste for the cutting unkindness of crystals—is easier and much less painful than their cure.

And so we end our crystal gazing, leaving a multitude of other faces and facets and edges for someone else to display. The pathologies of the crystal and the hypotheses of Life's initiation with the crystal were ours to scarcely touch. In connection with the crystal as the beginning of all things being, Carruth, in his fine poem "Each in his own tongue", builded better than he knew—for he, too, places the crystal before the cell. One of the stanzas of his much quoted poem affords the lecturer a splendid stopping place.

"A fire-mist and a planet,
A crystal and a cell,
A Jelly fish and a Saurian,
And caves where the cave-men dwell.
Then a sense of law and beauty
And a face turned from the clod,
Some call it evolution
And others call it God!"

ABSTRACTS FROM AND REVIEWS OF THE LITERATURE OF THE SCIENCES SUPPORTING PUBLIC HEALTH

Bacteriology . . . . Louis Gershenfeld, B. Sc., Ph. M.
Biology . . . . . Marin S. Dunn, Ph. D.
Chemistry . . . . . Arthur Osol, Ph. D.
Pharmacy . . . . . E. Fullerton Cook, Ph. M.
and their assistants

Warning Against Treatment of Induced Malaria with Mapharsen and Tryparsamide. M. D. Young and S. B. McLendon. *Pub. Health Rep. 54,* 1509 (1939). Arsenicals have been tried from time to time in the treatment of malaria. According to various reports such preparations as arsphenamine and neoarsphenamine relieve the symptoms of tertian malaria temporarily, but relapses are common. Against quartan and estivoautumnal malaria these arsenicals have been less successful and very little benefit has usually attended their use.

Mapharsen, a trivalent arsenic compound formed by the oxidation of any of the arsphenamines, has recently come into use in the treatment of syphilis. Goldman (*Am. J. Med. Sci. 196,* 502 (1938)) working with both natural and induced tertian malaria, used mapharsen to terminate the chills and fever with good results. Goldman states that this drug was immeasurably more effective than quinine for the treatment of malaria.

During the past year at the South Carolina State Hospital a series of ten paretics who had been infected with quartan malaria for therapeutic purposes were given mapharsen. Twenty-two weeks after the completion of mapharsen treatment, blood smears from all ten patients still showed parasites, although the patients showed no symptoms of malaria. The parasites were shown to be viable by reason of the fact that transplanting them into two uninfected persons brought about typical quartan malaria in these persons.

Examination was likewise made of three quartan malaria patients who had received tryparsamide. One year after completion of the tryparsamide treatment two patients still harbored the parasites and the third patient at the end of nine months.

These findings lead the authors to warn against the use of these drugs for this purpose, since malaria carriers who show no symptoms might be paroled from the hospital and in this way establish foci of infections for a type of malaria which is now rare in the United States. L. F. T.

The Toxicity of Parachlormetacresol and Phenyl Mercuric Nitrate. R. Wien. *Quart. J. Pharm. & Pharmacol. 12,* 212 (1939). In an investigation by Berry, Jensen and Siller (see abstract *Amer. J. Pharm.,* March, 1939) the recommendation was made of combining the use of heat and a bactericide for the sterilization of solutions of certain thermolabile substances intended for parenteral injection. It was suggested that 0.25-0.3 per cent. of parachlormetacresol or 0.002 per cent. phenyl mercuric nitrate should replace 0.5 per cent. phenol. These substances in the stated concentrations were found to accomplish a complete destruction of *B. subtilis* when such solutions were heated at 100 degrees C. for 30 minutes.

This recommendation was subject to satisfactory reports on the toxicity of these substances. The author reports on this phase of the work as follows: Parachlormetacresol has been shown to have about the same toxicity as phenol and phenyl mercuric nitrate the same order of toxicity as merthiolate. The 0.25 per cent. solution of parachlormetacresol is therefore unlikely to be more toxic than the 0.5 per cent. phenol which is widely used in injections, while phenyl mercuric nitrate (recommended for use in 0.002 per cent.) can be compared with merthiolate which has been used for some time in comparable dilutions as a bactericidal agent and has been claimed to be of low toxicity. The conclusion, therefore, is that the substances under consideration are likely to be harmful in practice in the concentrations suggested. L. F. T.

A Color Reaction for Sulfur. L. Van Itallie. *J. Pharm. Chem., Paris. 29,* 97 (1937), through *Quart. J. Pharm. & Pharmacol. 12,* 279 (1939). The reaction, previously reported by the author, between sulfur and pyridine solution and sodium hydroxide can be carried out either by adding a few drops of sodium hydroxide solu-

tion to a solution of the sulfur in pyridine or by shaking the sulfur with 1 or 2 cc. of the hydroxide solution and then adding pyridine. A green color is first produced, but by the addition of more hydroxide in the former case, or more pyridine in the latter, a characteristic blue coloration is produced, this color, however, is not persistent. The test can be used for the identification of sublimed, precipitated or colloidal sulfur and is sensitive to 0.005 mgm. L. F. T.

Heparin. *Pharm. J. 88,* 642 (1939). In 1772 Hewson observed that tissue from the large blood vessels delayed the normal coagulation of the blood. Howell in 1928 found that a potent substance possessing this property was in the liver. This substance which he named heparin was also isolated from other organs.

Several workers have contributed to our present knowledge of its chemical nature and its properties are in agreement with what is known of its constitution. The potency of heparin is unaffected by ordinary enzymes, oxidizing or reducing agents. It is resistant to heat and may be sterilized in an autoclave.

One milligram of the pure substance is sufficient to prevent coagulation of about 500 cc. of cat's blood for 24 hours at 0 degrees C. In transfusion it may be added to the blood after it is withdrawn from the donor or it may be injected into the donor before it is removed. Chemically pure heparin injected intravenously into animals and man causes no ill effects. The action is rapid; five minutes after intravenous injection blood can be taken from the donor without any danger of clotting during the transfusion. Heparin soon passes from the blood and is stored in the tissue before excretion in the urine so that heparinization of the donor does not last for long. This is important since if the donor remains about one and a half hours in the hospital before leaving his normal clotting time is completely reestablished. It is of course quite necessary that the donor have no open wounds, stomach or other ulcers, hemorrhoids, etc.

The dose required for both animals and humans is the same, namely, 1 mg. 1 kg. body weight. This dose raises the coagulation time to 30-45 minutes.

Heparin is likewise being investigated for the prevention of thrombi following certain surgical operations, as an addition to blood

in performing the sedimentation reaction of the cells, and other routine blood chemistry tests.

Natural and Artificial Soft Paraffins (Petrolatums). H. Brindle. *Pharm. J. 89,* 93 (1939). Soft paraffin is defined in the B. P. as a mixture of semi-solid hydrocarbons obtained from petroleum. This description excludes mixtures of liquid and hard paraffins known as "artificial" or soft paraffin. Strictly interpreted it would also exclude "natural" soft paraffin containing any proportion of liquid or solid paraffins. It is obviously impossible to insist upon so strict an interpretation since the purest so-called "natural" soft paraffin must contain hydrocarbons of low and fairly highly melting points or different degrees of solidity and it would be difficult to decide in some cases where to draw the line between semi-solid and solid even if it were possible to separate the constituents. Nevertheless, in spite of the required standards, there is a very undesirable variation in the character of soft paraffins which are supplied as of official quality. The difference is not usually a matter of melting point or refractive index so that such tests could not bring about anything approaching uniformity.

The author has devised a method for determining the critical solution temperature of soft paraffin in a mixture of carbon tetrachloride and glacial acetic acid. The volumes of crystalline deposit, if any, and of the upper oily layer which separates are also determined. Freedom from adulteration with liquid paraffin and hard paraffin is indicated by (1) a high critical solution temperature (2) a low volume of crystalline deposit and (3) a considerable volume of separated upper oily layer.

The results obtained with thirty-six commercial samples are reported as well as those given with laboratory prepared samples of fictitious soft paraffin. The author believes the test enables one to distinguish true and artificial soft paraffins. L. F. T.

A Note on the Stabilization of Hydrogen Peroxide for Pharmaceutical Purposes. S. M. Triton. *Pharm. J. 89,* 103 (1939).

Hydrogen peroxide as sold for pharmaceutical purposes varies considerably in its efficacy. Especially in hospital pharmacies complaints are frequently received that the solution has lost its strength. It has been reported that the addition of very small quantities of ferric or cupric sulfate, salts which catalyze the decomposition of hydrogen peroxide, greatly increase its germicidal effect against *B. coli.* Thus hydrogen peroxide which exhibited a phenol coefficient of 0.014 had its activity increased 100 times by the addition of 0.1 millimol of the respective salt to each 120 cc. of peroxide.

It is important that hydrogen peroxide should decompose easily in the presence of organic matter and, consequently, a test solution containing the enzyme catalase which is present in blood, pus, and saliva was prepared as follows: Half a pound of fresh calf's liver was chopped up and allowed to stand in a refrigerator with 500 cc. of chloroform water overnight and then the solution filtered. By diluting this solution ten times a suitable concentration was obtained for testing various solutions of hydrogen peroxide.

Numerous solutions of hydrogen peroxide containing different added preservatives were tested for their rate of oxygen liberation in the presence of a weak solution of catalase.

Commercial peroxides stabilized with acid gave up very little oxygen in comparison with other peroxides which contained neutral stabilizers. It was also found that unstabilized products varied in their performance probably due to traces of persulfate.

Stabilizers which were studied included acetanilide, phenazone, benzoic acid, thiourea, urea, and hexamine. They were added to standard hydrogen peroxide solution in a concentration of 0.1 per cent. and their suitability determined insofar as their capacity to neutralize the enzyme catalase was concerned.

The results showed urea to be a suitable stabilizer with phenazone a good second. It is advisable to discontinue the stabilization of peroxide with sulfuric acid. L. F. T.

BOOK REVIEW

Done by persons, unafraid to upbraid, but perfectly willing to give praise where praise is really due.

Standard Chemical and Technical Dictionary. H. Bennett. 638 pages + xlii (Introduction). $10.00. Chemical Publishing Co., New York, 1939.

The major portion of this volume is devoted to an alphabetical arrangement of chemical, physical, mathematical and technical terms which are briefly defined or described as best suits each individually. Preceding this are several chapters in which the use of the Dictionary is described, the nomenclature of organic compounds explained, the many prefixes, abbreviations and contractions commonly employed are presented. The last few pages of the book are devoted to the meaning of numerous symbols.

Although the reviewer realizes the immensity of the task involved in gathering the data required in compiling such a dictionary, he cannot speak for its up-to-date coverage as claimed by its publishers. Taking at random several important advances in the last several years: coacervation, molecular distillation, oestrone, vitamin K, sulfanilamide, not one is found mentioned in the text. Furthermore, certain of the definitions are not considered accurate, e. g., bone gelatin "gelatin made from clean bones of heads and feet." Such a definition is surely not acceptable to one who is familiar with the raw material used in a gelatin plant. The misconception that gelatin is made from the feet of cattle was dispersed a decade ago.

In all the Dictionary is useful as a reference but not sufficiently broad in its scope and coverage to meet the need for which it is intended.

L. F. Tice.